--Alpha-9 integrin modulatory compounds identified and selected in accordance with the present invention find use in a number of disorders associated with alpha-9 integrin activity. Particularly, in view of discoveries described herein with respect to the neutrophil localization of alpha-9 integrin, as well as its ability to interact with VCAM-1, it is appreciated that alpha-9 integrin inhibitory compounds will find particular utility in the treatment of a variety of disorders which include an inflammatory component, particularly those to which the inflammatory component is associated with VCAM-1 binding to alpha-9 integrin.--

IN THE CLAIMS:

Please cancel claims 24-30 without prejudice to or disclaimer of the subject matter contained therein.

Please replace Claims 31, 32, 34, and 36 with amended Claims 31, 32, 34, and 36 as follows:

31. (Amended) The method of Claim 37, wherein the disorder is an inflammatory condition.

32. (Amended) The method of Claim 31, wherein said inflammatory condition is characterized by increased neutrophil activity.

34. (Amended) The method of Claim 31, wherein said alpha-9 integrin antagonist compound exhibits a potency in inhibiting binding between alpha-9 integrin and an alpha-9 integrin ligand that is at least 1/1000 as high as an inhibitory potency exhibited by a compound selected from the group consisting of:

N-(toluene-4-sulfonyl)-L-prolyl-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-prolyl-L-4(N,N-dimethylcarbamyloxy)phenylalanine,

N-(1-methylpyrazole-4-sulfonyl)-L-prolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl-)-L-(1,1-dioxo-5,5-dimethyl)thiaprolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-N-methyl-L-alaninyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-[(1,1-dioxo)thiamorpholin-3-carbonyl]-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)prolyl-4-(piperazinoyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)sarcosyl-4-(N,N-dimethylcarbamyloxy)phenylalanine, and

N-(toluene-4-sulfonyl)-L-(5,5-dimethyl)thiaprolyl-L-4-[3-(N,N-dimethyl)propoxy]phenylalanine.

36. (Amended) The method of Claim 31, wherein said alpha-9 integrin antagonist is selected from the group consisting of:

N-(toluene-4-sulfonyl)-L-prolyl-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-prolyl-L-4(N,N-dimethylcarbamyloxy)phenylalanine,

N-(1-methylpyrazole-4-sulfonyl)-L-prolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl-)-L-(1,1-dioxo-5,5-dimethyl)thiaprolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-N-methyl-L-alaninyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-[(1,1-dioxo)thiamorpholin-3-carbonyl]-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)prolyl-4-(piperazinoyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)sarcosyl-4-(N,N-dimethylcarbamyloxy)phenylalanine, and

N-(toluene-4-sulfonyl)-L-(5,5-dimethyl)thiaprolyl-L-4-[3-(N,N-dimethyl)propoxy]phenylalanine.

Please add new Claims 37 – 47 as follows.

37. (New) A method of treating a disorder, involving binding of alpha-9 integrin to an alpha-9 integrin ligand, in a mammalian subject comprising administering to a mammalian subject in need thereof a pharmaceutically effective dosage of an alpha-9 integrin antagonist compound.

38. (New) The method of Claim 37, wherein the alpha-9 integrin ligand is vascular cell adhesion molecule-1 (VCAM-1).

39. (New) The method of Claim 37, wherein the alpha-9 integrin antagonist compound binds ligands selected from the group consisting of osteopontin, tenascin, VCAM-1, and combinations thereof.

40. (New) The method of claim 31, wherein the inflammatory condition is selected from the group consisting of chronic asthma, smooth muscle cell proliferation in atherosclerosis, vascular occlusion following angioplasty, fibrosis and glomerular scarring as a result of renal disease, aortic stenosis, hypertrophy of synovial membranes in rheumatoid arthritis, and inflammation and scarring that occur with the progression of ulcerative colitis, and Crohn's disease.

41. (New) A method for inhibiting binding of alpha-9 integrin to an alpha-9 integrin ligand in a mammalian subject, the method comprising administering to a mammalian subject in need thereof a pharmaceutically effective dosage of an alpha-9 integrin antagonist compound.

42. (New) The method of Claim 41, wherein the alpha-9 integrin ligand is vascular cell adhesion molecule-1 (VCAM-1).

43. (New) The method of Claim 41, wherein said alpha-9 integrin antagonist compound is a selected from a group of compounds which inhibit alpha-4/beta-1 integrin binding to vascular cell adhesion molecule-1 (VCAM-1).

44. (New) The method of Claim 41, wherein said alpha-9 integrin antagonist compound exhibits a potency in inhibiting binding between alpha-9 integrin and an alpha-9 integrin ligand that is at least 1/1000 as high as an inhibitory potency exhibited by a compound selected from the group consisting of:

N-(toluene-4-sulfonyl)-L-prolyl-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-prolyl-L-4(N,N-dimethylcarbamyloxy)phenylalanine,

N-(1-methylpyrazole-4-sulfonyl)-L-prolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl-)-L-(1,1-dioxo-5,5-dimethyl)thiaprolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-N-methyl-L-alaninyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-[(1,1-dioxo)thiamorpholin-3-carbonyl]-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)prolyl-4-(piperazinoyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)sarcosyl-4-(N,N-dimethylcarbamyloxy)phenylalanine, and

N-(toluene-4-sulfonyl)-L-(5,5-dimethyl)thiaprolyl-L-4-[3-(N,N-dimethyl)propoxy]phenylalanine.

45. (New) The method of Claim 41, wherein said compound is selected from the group consisting of carbamyl compounds having the formula: R^1-SO_2-NR^2-CHR^3-Q-CHR^5-CO_2H wherein

R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R^2 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and R^1 and R^2 together with the nitrogen atom bound to R^2 and the SO_2 group bound to R^1 can form a heterocyclic or a substituted heterocyclic group;

R^3 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and, when R^2 does not form a heterocyclic group with R^1, R^2 and R^3 together with the nitrogen atom bound to R^2 and the carbon atom bound to R^3 can form a heterocyclic or a substituted heterocyclic group;

R^5 is $-(CH_2)_x-Ar-R^{5'}$ where $R^{5'}$ is selected from the group consisting of

$-O-Z-NR^8R^{8'}$ and $-O-Z-R^{12}$ wherein R^8 and $R^{8'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, and where R^8 and $R^{8'}$ are joined to form a heterocyclic or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of

$-C(O)-$ and $-SO_2-$,

Ar is aryl, heteroaryl, substituted aryl or substited heteroaryl,

x is an integer of from 1 to 4;

Q is $-C(X)NR^7-$ wherein R^7 is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur; and

pharmaceutically acceptable salts thereof.

46. (New) The method of Claim 41, wherein said alpha-9 integrin antagonist is selected from the group consisting of:

N-(toluene-4-sulfonyl)-L-prolyl-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-prolyl-L-4(N,N-dimethylcarbamyloxy)phenylalanine,

N-(1-methylpyrazole-4-sulfonyl)-L-prolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl-)-L-(1,1-dioxo-5,5-dimethyl)thiaprolyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-N-methyl-L-alaninyl-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-[(1,1-dioxo)thiamorpholin-3-carbonyl]-L-4-(N,N-dimethylcarbamyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)prolyl-4-(piperazinoyloxy)phenylalanine,

N-(N-*p*-toluenesulfonyl)sarcosyl-4-(N,N-dimethylcarbamyloxy)phenylalanine, and

N-(toluene-4-sulfonyl)-L-(5,5-dimethyl)thiaprolyl-L-4-[3-(N,N-dimethyl)propoxy]phenylalanine.

47. (New) The method of Claim 33, wherein said alpha-4/beta-1 integrin ligand is vascular cell adhesion molecule-1 (VCAM-1).